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—Editorial—

Early Recognition of Tuberculosis

The community-wide survey is such a new activity in this country that its fruits have just begun to appear. This issue presents, in a paper by Roemmich, et al, some of the findings of one of these mass X-ray surveys. Although this is but a preliminary report of the Minneapolis survey, presenting an analysis of the first 1,500 of a total of 6,000 persons referred for study, the material is sufficient to forecast the final results.

In conducting its follow-up, Minneapolis has demonstrated beyond question that proper follow-up can be done in the wake of such surveys. So thorough and conscientious was the follow-up effort on the part of private practitioners and the health department that two-thirds of the cases judged tuberculous (of which a large number was, of course, inactive) had the benefit of bacteriological study. Phthisiologists have long agreed that the diagnosis of tuberculosis must rest upon the laboratory demonstration of tubercle bacilli in tuberculous suspects. Here, then, is an instance of the integration of prescription and action, and one which furnishes abundant proof of the feasibility of complete diagnostic procedure.

As will be seen in the Minneapolis report, the proportion of previously unrecognized cases found among the 1,500 suspects studied was huge. We are told that 648 of this group were diagnosed as tuberculous, and that 98 of these, or 15.1 percent, had active disease. Moreover, only 9 of these active cases were previously known to the health department.

*This is the thirty-second of a series of special issues of PUBLIC HEALTH REPORTS devoted exclusively to tuberculosis control, which will appear the first week of each month. The series began with the Mar. 1, 1946 issue. The articles in these special issues are reprinted as extracts from the PUBLIC HEALTH REPORTS. Effective with the July 5, 1946 issue, these extracts may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 10 cents a single copy. Subscriptions are obtainable at $1.00 per year; $1.25 foreign.

How long it would have taken to discover these previously unknown cases through routine channels, is of course open to conjecture, for, despite the presence of definite active disease, an appreciable number of them were symptomless. As for the rest of the hidden cases, signs and symptoms were few and minor, so that until that time they had not consulted a physician. Nor, indeed, could we have relied on contact investigations to bring about the discovery of any significant number of these persons, for only three could give any history of exposure to a case of tuberculosis.

Certainly, we are well aware of the penalties of delay in diagnosing tuberculosis. Undiscovered, the disease progresses, often to the point of hopeless intractability; unchecked, it spreads freely; and unrecognized, it breeds new cases. If we are to succeed in controlling tuberculosis, this is exactly what must not continue to occur. Chadwick and Pope summarize the case for the routine chest examination of healthy persons when they say: "Early recognition, still the most important factor in prognosis, becomes even more significant as the first step in breaking the chain of infections."

The prime lesson of the Minneapolis experience is that we must increase our "index of suspicion," and must learn to think of tuberculosis as a possibility in all persons who have not had recent chest examinations. Moreover, in those cases revealed to have X-ray evidence of infection, follow-up can and must be as vigorous and complete as that which has been so wisely prosecuted in Minneapolis.

FRANCIS J. WEBER, *Medical Director*,[1]
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Preliminary Report on a Community-Wide Chest X-Ray Survey at Minneapolis, Minnesota

By William Roemmich, *S. A. Surgeon*,[1] Francis J. Weber, *Medical Director*,[2] Frank J. Hill, M. D.,[3] and Lucille Amos, *Reporting Methods Analyst* [2]

An intensified chest X-ray survey was conducted in Minneapolis, Minnesota, from May 5 to August 25, 1947. The purpose was to X-ray the chest of every person 15 years of age or over, as a procedure for finding cases of tuberculosis, lung or respiratory cancer, heart abnormalities and other chest diseases. The survey was jointly sponsored by the Minneapolis Health Department, the Hennepin County Medical Society, the Hennepin County Tuberculosis Association, the Minnesota State Cancer Society, and the Hennepin County Chapter of the American Red Cross. The undertaking was conducted in cooperation with the Minnesota State Department of Health, the Glen Lake Sanatorium Commission, and the United States Public Health Service.

Eleven mobile and portable 70 mm. photofluorographic units were used to screen the population. In addition, one X-ray unit took 14″ x 17″ celluloid roentgenograms to confirm or disprove the 70 mm. impressions. This report shows the radiological findings and the first 1,500 clinical evaluations. The screening process involving the use of 70 mm. X-ray film followed by 14″ x 17″ confirmatory film, has been completed. The results of clinical study are only partially known.

Screening Process

Between May 5 and August 25, 1947, 306,020 X-rays were taken by the 70 mm. X-ray units. Of these 4,507 or 1.5 percent were unsatisfactory. Of the satisfactory exposures 96.6 percent were "negative" while 3.4 percent were "positive" and in need of further study (table 1).

Table 1. *70 mm. film findings*

Reading	Number	Percent
Total satisfactory exposures	301, 513	100. 0
Negative	291, 275	96. 6
Suspected tuberculosis	5, 977	2. 0
Suspected other chest disease	4, 261	1. 4

[1] Tuberculosis Control Division, Public Health Service, Acting Tuberculosis Control Officer.
[2] Tuberculosis Control Division, Public Health Service.
[3] Minneapolis Commissioner of Health.

Persons having "positive" screening film readings (except 841 of the 858 "cardiacs") were recalled for a 14" x 17" film. Altogether 9,236 persons were given appointments for a 14" x 17" confirmatory X-ray film. (Included in table 1, are 161 instances of duplicate "positive" 70 mm. films and instances of other referrals for a confirmatory film). Of the 9,236 persons recalled, 8,333 had responded by January 5, 1948.

Radiological impressions on 14" x 17" films are shown in table 2.

Table 2. *14" x 17" film findings*

Reading	Number	Percent	Percent
Total 14" x 17" films taken	8, 333	100. 0	
Essentially negative	2, 331	28. 0	
Positive	6, 002	72. 0	100. 0
Suspected tuberculosis	3, 850	46. 2	64. 1
Suspected other pathology	2, 152	25. 8	35. 9

It may be seen that 28 percent of the 14" x 17" films taken were read "essentially negative," while the remaining 6,002 or 72 percent indicated the need of further study.

Of the 3,850 confirmatory films in which tuberculosis was suspected 3,627 or 94.2 percent were classified as to stage of disease (table 3). Only 15.2 percent of these lesions appeared to be in an advanced stage.

Table 3. *Tuberculosis by stage of disease, 14" x 17" films*

Impression	Number	Percent
Total	3, 627	100. 0
Minimal	3, 077	84. 8
Moderately advanced	481	13. 3
Far advanced	69	1. 9

Table 4 shows the result of checking the names of the 3,850 persons suspected of having tuberculosis, on the basis of their 14" x 17" film (shown in table 2), against the local tuberculosis case register.

Table 4

	Number	Percent
Total suspected tuberculosis	3, 850	100. 0
Not on local register	3, 497	90. 8
On local register	353	9. 2

EPIDEMIOLOGICAL RECORD

Date _____ Case No. _____

1. Name _____
   Last First Middle (Maiden)
2. Address _____ Census tract _____ Phone _____
3. Birthdate _____ Age _____ Sex _____ Race _____ Marital Status _____
   Mo. Day Yr.
4. Consort's name _____
5. State or country of birth _____ State or country of longest residence _____ No. of yrs. _____
6. Present work _____ No. of yrs. _____ Former work _____ No. of yrs. _____
7. Residence city or county since _____ Previous address _____
   year
8. Person most likely to locate you in case you move? _____
   Rel. to patient _____ Address _____ Phone _____
9. Have you ever had TB? No _____ Yes _____ Year _____ Treatment: None _____
   Pr. phys. _____ Cl. _____ San. _____
10. Did you live in household with tuberculosis? No _____ Yes _____ How long? _____
11. Did anyone in your home die of TB? No _____ Yes _____ When _____ Relationship _____
12. Have you had recent illness? No _____ Yes _____ Specify _____
    Temp: No _____ Yes _____ Amt. _____ Wt. loss: No _____ Yes _____ Amt. _____
    Fatigue: No _____ Yes _____
13. Did you ever have chest X-ray taken? No _____ Yes _____ Date last X-ray _____
    Why taken? _____ Where? _____
14. Physician's name _____ Address _____
15. When was the last time you saw your physician? _____
16. Remarks _____

17. 70 mm. reading
    Film No. _____
    Date _____
    N U T S O

    14" x 17" reading _____ Film No. _____
    Date _____
    Tuberculosis _____ Cardiac _____ Other _____

18. Stage of disease: M _____ MA _____ FA _____ Other _____
19. Impression of activity: Active _____ Inactive _____ Questionable _____
20. Source of first report _____
21. CONTACTS

	Name (address if different from case)	Relation	Age	Sex	TB history	Date of X-ray
1.						
2.						
3.						
4.						
5.						

DOCTOR'S RECORD ONLY

22. Tubercle bacilli: Present _____ Absent _____ Date _____
    Sputum: Smear _____ Conc. _____ Culture _____ No sputum _____
    Gastric culture _____ No examination made _____
23. Tuberculin test: Date applied _____ Date read _____
    O. T. 1st dose _____ Induration in mm _____ 2d dose _____ Induration in mm _____
    P. P. D. 1st dose _____ Induration in mm _____ 2d dose _____ Induration in mm _____
24. Symptoms: Fever: Yes _____ No _____ Fatigue: Yes _____ No _____
    Weight loss: Yes _____ No _____ Others: Yes _____ No _____
25. Is there any evidence for extra pulmonary tuberculosis? Specify _____
26. If nontuberculosis, what was final diagnosis? _____
27. What disposition has been made of patient? _____
28. Do you wish PHN supervision? Yes ____ No ____ If none, state reason _____
29. Diagnosis _____ Signature _____
30. Remarks _____

Only 9.2 percent of these persons were previously registered with the health department as cases of tuberculosis.

For each of the persons who returned for a 14″ x 17″ film, an Epidemiological Record was prepared (page 1287). In the 6,002 instances where the 14″ x 17″ radiological impression was "positive," a copy of this Epidemiological Record was submitted to the individual's private physician, for 70 percent of the cases, and to the public health center clinic in 30 percent of the cases (table 5). When

Table 5

Total positive referred	6,002
Referred to private physician	4,219
Referred to public clinic	1,783

clinical study was finished lines 22 through 30 under "Doctor's Record Only," were completed, indicating the result of clinical and bacteriological follow-up. The record was then returned to the health department.

Clinical Evaluation

Through the courtesy of the Northwestern National Life Insurance Company, information from the Epidemiological Records which were returned to the health department is being coded and cards are being punched for machine tabulation. Some of the information from the first 1,500 Epidemiological Records was sent to the health department; it is tabulated in table 6.

Table 6. *Clinical diagnoses on the first 1,500 returns out of 6,000 referrals*

	Number	Percent
Total records returned	1,500	100.0
Negative chest	159	10.6
Diagnosis tuberculosis	648	43.2
Diagnosis other chest disease	585	39.0
No diagnosis made	108	7.2

A complete breakdown of information appearing under "Other Chest Disease" group is not available.

Table 7 shows the extent of bacteriological study as reported on line 22 of the Epidemiological Record for the 648 persons on whom a diagnosis of tuberculosis was made. It is of interest that 66 percent of the cases of tuberculosis reported on the first 1,500 Epidemiological Records were studied bacteriologically. Of the 428 so studied, 35

percent (151) were studied by sputum smear, 44 percent (192) by sputum culture and 21 percent (85) by gastric culture. Of the total group studied bacteriologically, 79 or 19 percent were found to be "positive" for tubercle bacilli. In addition to these 79 cases classed as active on the basis of bacteriological study, there were 19 cases considered active on the basis of X-ray changes and clinically consistent with active tuberculosis.

Table 7

	Number	Percent
Total diagnosed tuberculosis	648	100. 0
Studied bacteriologically	428	66. 0
Not studied bacteriologically	220	34. 0

The stage and activity of disease of the 648 persons diagnosed as having tuberculosis are shown in table 8. Of the 98 active cases of

Table 8. *Stage and activity of disease of first 648 cases clinically diagnosed as tuberculosis*

	Total		Minimal		Moderately advanced		Far advanced		Other	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Total	648	100.0	463	100.0	121	100.0	23	100.0	41	100.0
Active	98	15.1	39	8.4	49	40.5	9	39.1	1	2.4
Questionably active	17	2.6	10	2.2	6	5.0	0	0.0	1	2.4
Inactive	533	82.3	414	89.4	66	54.5	14	60.9	39	95.1

tuberculosis (table 8), nine were previously registered with the health department. Of these nine, six were being carried on the active register and three were being carried on the inactive register. An additional nine persons with active tuberculosis admitted history of tuberculosis (line 9 of the Epidemiological Record) but were not known to the health department. Eighty were new cases of tuberculosis. Of these, 25 had neither contacts nor symptoms. They could have been found only with case-finding methods such as roentgenological study, fluroscopic study or tuberculin testing on a mass basis. The remaining 55 out of 80 new cases had signs or symptoms (line 24 of the Epidemiological Record). We may suppose but have no assurance that these were related to their tuberculosis. Apparently the signs or symptoms were not severe enough to cause the individual to seek medical attention. Only three reported that they had been in contact with a case of tuberculosis (line 10 of the Epidemiological Record). Of the 80 new cases of tuberculosis discovered,

only three could have been found through contact examination providing contact had occurred in their place of residence or had been reported to it.

As of February 15, 1948, 55 of the 98 persons with active tuberculosis had entered a sanatorium, as is shown in table 9. No one was excluded from the sanatorium on basis of bed shortage. Of the active cases hospitalized, 30.9 percent were minimal, 56.4 percent were moderately advanced and 12.7 percent were far advanced.

Table 9. *Disposition of first 98 active cases*

Stage of disease	Total	In sanitarium	At home
Total	98	55	43
Minimal	39	17	22
Moderately advanced	49	31	18
Far advanced	9	7	2
Other	1	0	1

Depression of Tuberculin and Histoplasmin Sensitivity Associated With Critical Illness[1]

By Michael L. Furcolow, *Surgeon;* Mabel E. Emge, *S. A. Nurse Officer;* and Ivan L. Bunnell, *S. A. Surgeon, Public Health Service*

A project was organized in March 1947, to study nontuberculous pulmonary lesions in hospital patients coming to autopsy. The original plan was to give tuberculin and histoplasmin skin tests to a large number of critically ill patients. Skin sensitivity was to be correlated with subsequent autopsy findings on those who died. As the skin tests were made among the group of critically ill patients, it soon became evident that the number of reactors to each antigen was considerably smaller than the number expected on the basis of tests previously performed on healthy adults in the same city. A review of the preliminary findings led to the establishment of the hypothesis that depression of skin sensitivity to both antigens is associated with critical illness from any cause. The testing of this hypothesis and its elaboration comprise the subject matter of this report.

Methods and Materials

The study was conducted from March 1947 through December 1947 at the Kansas City General Hospital, a municipal hospital serving

[1] From the Office of Field Studies, Tuberculosis Control Division.

white residents of Kansas City, Mo. Except for patients receiving pediatric treatment, all those listed as critically ill by resident physicians were skin-tested with tuberculin and histoplasmin. The patients ranged in age from 20 to over 80, with the majority 60 and over. Some patients suffered from acute conditions such as fractures, burns, concussions, and acute infections. These were predominant among the young (69 percent in the 20–29 year age group). Chronic diseases—malignant tumors, cardiac decompensation, chronic infections—predominated in the older groups (73 percent of age group 80 and over).

Skin tests were performed with tuberculin and histoplasmin by the intracutaneous (Mantoux) method. The histoplasmin (H–15) was prepared and titered for potency by Dr. Arden Howell of the Public Health Service, and was given in a dose of 0.1 cc. of 1/1000 dilution. The tuberculin used was PPD-S furnished by Dr. Florence Seibert of the Henry Phipps Institute, Philadelphia, Pa., and was administered in a single dose of 0.0001 mgm. in 0.1 cc. of diluent. Reactions in which the area of induration measured 5 mm. or more in diameter at the 48-hour reading were considered positive.

Wherever possible, reactions were read at 24- 48- and 72-hour intervals, but only the records of those read at 48 hours were included in the study for the sake of uniformity. The records of 16 patients with active tuberculosis and one with histoplasmosis were also excluded, for it is already known that sensitivity to both tuberculin and histoplasmin often declines in the last stages of these diseases (*1*, *2*, *3*). Since all patients admitted to this hospital are routinely X-rayed, it is probable that these 17 cases were the only ones with detectable active tuberculosis and histoplasmosis among the entire critically ill group. With these exclusions, the records of 305 patients were available for analysis in this study.

To provide proper bases for comparison, norms were obtained from the results of tuberculin and histoplasmin tests of approximately 5,000 presumably healthy adults in Kansas City (*4*). These persons were employees of large industrial or mail-order firms, city employees, and residents of homes for the aged and indigent. Sensitivity rates for this apparently healthy group were developed by age and sex for each antigen.

Results

Table 1 shows the number and percentage of positive reactors to tuberculin and histoplasmin for selected age groups among critically ill and apparently healthy people. The percentages are graphically presented in figure 1.

The rate of tuberculin sensitivity in the general population rises

Table 1. *Tuberculin and histoplasmin reactors among critically ill and apparently healthy persons in selected age groups, Kansas City, Mo.*

Age	Critically ill					Apparently healthy				
	Number tested	Tuberculin reactors		Histoplasmin reactors		Number tested	Tuberculin reactors		Histoplasmin reactors	
		Number	Percent	Number	Percent		Number	Percent	Number	Percent
20–39	46	15	33	26	57	2,917	925	32	2,328	80
40–59	78	14	18	32	41	1,233	854	69	970	79
60–79	133	22	17	28	21	348	273	78	235	68
80 and over	48	3	6	8	17	57	37	65	44	77
Total	305	54		94		4,555	2,089		3,577	

rather sharply from 32 percent positive in the 20–39 year age group to 78 percent in persons 60 to 79. From that peak it appears to drop to 65 percent positive in the oldest group, 80 and over. In contrast to these relatively high rates, the tuberculin sensitivity rate for critically

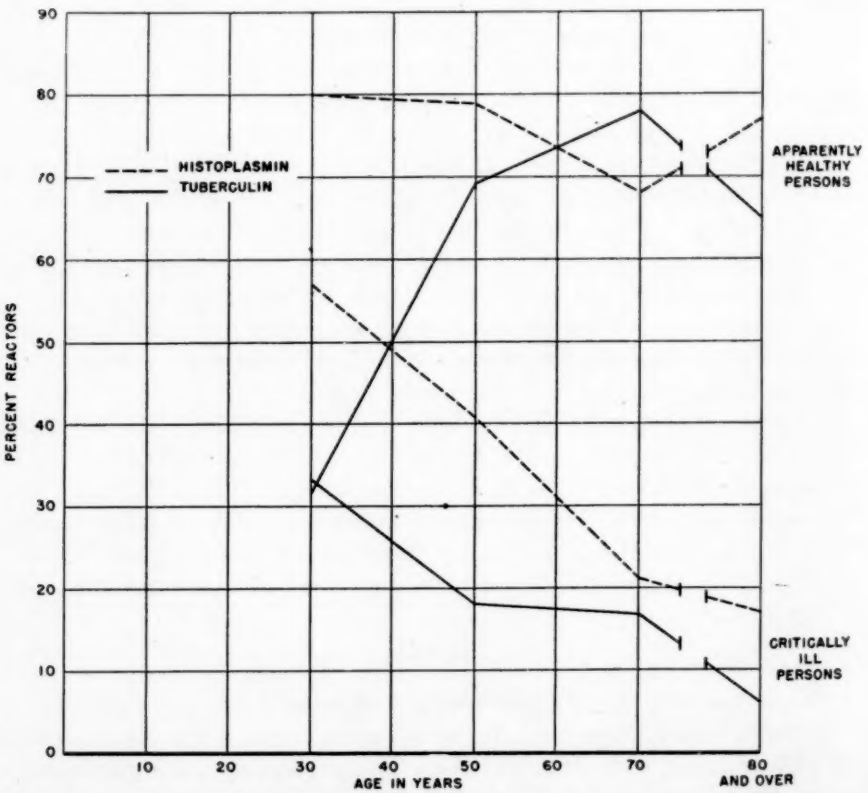

Figure 1. Percent of histoplasmin and tuberculin reactors among critically ill and apparently healthy persons in selected age groups, Kansas City, Mo.

ill patients, while approximately the same (33 percent positive) in the youngest age group, falls to a low of 6 percent in the oldest group. It is therefore evident that tuberculin sensitivity rates are much lower (except among 20–29 year-olds) for critically ill patients than for apparently healthy residents of Kansas City.

Histoplasmin sensitivity in apparently healthy persons is high—near 75 percent—in every age group. But the curve of histoplasmin sensitivity for the critically ill falls steadily and fairly sharply from a high of 57 percent positive in the youngest age group to a low of 17 percent in the oldest.

Table 2. *Observed and expected reactors to tuberculin and histoplasmin, by age, among critically ill patients, and ratio of observed to expected reactors*

Age	Number tested	Tuberculin reactors			Histoplasmin reactors		
		Observed	Expected	$\frac{\text{Observed}}{\text{Expected}} \times 100$	Observed	Expected	$\frac{\text{Observed}}{\text{Expected}} \times 100$
20–39	46	15	14.7	102	26	36.8	71
40–59	78	14	53.8	26	32	61.6	52
60–79	133	22	103.7	21	28	90.4	31
80 and over	48	3	31.2	10	8	37.0	22
Total	305	54	203.4	27	94	225.8	41

Table 2 and figure 2 compare the number of reactors observed in the study group of critically ill patients and the number that would be expected on the basis of rates prevailing in the general population.

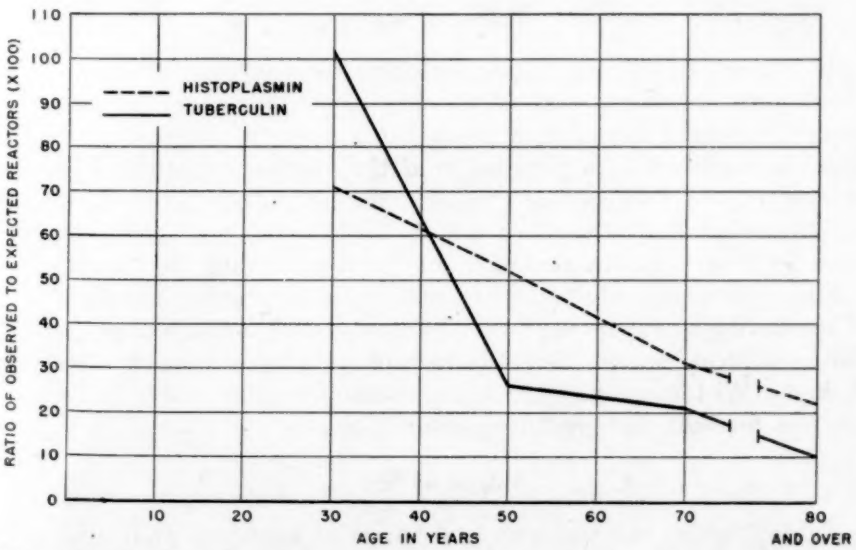

Figure 2. Ratio of observed to expected reactors to histoplasmin and tuberculin among critically ill persons in selected age groups, Kansas City, Mo.

As can be seen in table 1, the numbers of persons tested in the different age groups among the healthy are not proportionate to those tested in the same groups among the critically ill. Young people predominate in the general population, while old people are in a majority in the study group. In order to compensate for the differences in composition of the two groups, adjustment was made in the following manner. The percentage of reactors in each age group of the general population was applied to the total number of critically ill in corresponding age groups to arrive at the expected number of positive reactors among the critically ill. The expected number thus obtained was then compared with the actual number found. For example, 80 percent of 2,917 persons 20–39 years of age in the general population reacted to histoplasmin. Applying this percentage to the 46 persons of the same age among the critically ill yields 36.8 for the expected number of reactors, as against 26 actually observed.

The last column of table 2 shows the ratio of those actually found to those expected, expressed as percentages. Therefore, following through on the example given above, the ratio of 71 is arrived at from the calculation: $\frac{26}{36.8} \times 100$.

In the whole group of critically ill there were 94 observed histoplasmin reactors as compared with 225.8 expected, or 41 percent. The comparison between observed and expected tuberculin reactors for the group as a whole is even more striking. Here, only 54 were observed, as against 213.4 expected—a ratio of 27 percent.

Effect of Age

As indicated in figure 1, skin sensitivity during critical illness declines more markedly with advancing age. This point is perhaps better illustrated by figure 2 where the number of reactors actually found is expressed as a percentage of the number expected for each antigen in the various age groups. The downward slope of both curves is evidence of the effect of age. In the youngest age group the ratio for tuberculin reactors is about 100 percent, and that for histoplasmin reactors is about 71 percent. This indicates that the rate of sensitivity to tuberculin is not affected in the youngest age group during critical illness. But the histoplasmin rate already shows a decline. With increasing age, the proportion of observed to expected reactors for both antigens decreases.

Effect of Sex

Table 3 gives the numbers and ratios of observed and expected reactors to tuberculin and histoplasmin among the critically ill by age and sex. The data show that, in general, the rate of sensitivity

to both antigens is higher among males than among females, whether sick or well; further, that with advancing age, sensitivity to either antigen declines among the critically ill regardless of sex.

Table 3. *Observed and expected reactors to tuberculin and histoplasmin, by age and sex, among critically ill patients, and ratio of observed to expected reactors*

MALE

Age	Number tested	Tuberculin reactors			Histoplasmin reactors		
		Observed	Expected	$\frac{\text{Observed}}{\text{Expected}} \times 100$	Observed	Expected	$\frac{\text{Observed}}{\text{Expected}} \times 100$
20–39	24	10	9.8	102	15	19.7	76
40–59	52	12	39.0	31	23	42.1	55
60–79	88	17	70.6	24	18	58.4	31
80 and over	29	2	20.8	10	5	22.6	22
Total	193	41	140.2	29	61	142.8	43

FEMALE

20–39	22	5	5.7	88	11	17.2	64
40–59	26	2	15.9	13	9	19.5	46
60–79	45	5	32.6	15	10	32.0	31
80 and over	19	1	10.6	9	3	14.4	21
Total	112	13	64.8	20	33	83.1	40

Effect of Severity of Illness

Table 4 presents the numbers and ratios of observed to expected reactors among patients who survived their critical illness, in contrast to those for patients who died. If we assume that those who died were suffering from more severe illness than those who did not die, it appears that the more severe the illness, the smaller the number

Table 4. *Observed and expected reactors to tuberculin and histoplasmin, by age and outcome, among critically ill patients, and ratio of observed to expected reactors*

SURVIVED

Age	Number tested	Tuberculin reactors			Histoplasmin reactors		
		Observed	Expected	$\frac{\text{Observed}}{\text{Expected}} \times 100$	Observed	Expected	$\frac{\text{Observed}}{\text{Expected}} \times 100$
20–39	34	13	10.9	119	21	27.2	77
40–59	46	11	31.7	35	26	36.3	72
60–79	64	14	49.9	28	23	43.5	51
80 and over	13	3	10.1	30	2	10.0	20
Total	157	41	102.6	40	72	117.0	69

DIED

20–39	12	2	3.8	53	5	9.6	52
40–59	32	3	22.0	14	6	25.3	24
60–79	69	8	53.8	15	5	46.9	11
80 and over	35	0	22.7	0	6	26.9	22
Total	148	13	102.3	13	22	108.7	20

of reactors to skin tests. Among those who survived, the ratio of observed to expected reactors to histoplasmin was 69 percent, while among those who died it was 20 percent. For tuberculin, the survivors' ratio was 40 percent, and the others', 13 percent. The ratios for both antigens are thus seen to be more than three times greater among the survivors than among those who succumbed.

Some of those who died had been tested within a week of death; others more than a week before. The records of these patients were divided into two groups depending upon how long they had yet to live when their tests were made, again on the assumption that proximity of death is an index of severity of illness. Table 5 shows that

Table 5. *Number and percent of histoplasmin and tuberculin reactors among critically ill patients, by interval between test and death*

Days between test and death	Number tested	Histoplasmin reactors		Tuberculin reactors	
		Number	Percent	Number	Percent
7 days or less	76	7	9.0	5	6.5
More than 7 days	72	15	21.0	8	11.0

the patients nearest death—within 7 days—had a rate of sensitivity appreciably lower than those who had more than a week yet to live. Of the latter, 21 percent reacted to histoplasmin, while only 9 percent of the former were still able to react. For tuberculin, the rates were 11 percent and 6.5 percent, respectively.

Increase of Skin Sensitivity Rates with Recovery

Of the 157 survivors, 57 who remained in the hospital were retested at weekly intervals to see if sensitivity reappeared with returning health. The results of retesting are shown in table 6. With one exception, all those who were positive during critical illness remained positive. But 39 percent of those who were histoplasmin-negative and 42.5 percent of those who were tuberculin-negative converted to positive during the period of observation.

Table 6. *Results of retests on 57 critically ill patients, all ages combined* [1]

Original test	Total number retested	No change	Converters		Reverters	
			Number	Percent	Number	Percent
H+	19	19	0	----------	0	----------
T+	10	9	0	----------	[2] 1	10
H−	38	23	15	39.4	----------	----------
T−	47	27	20	42.5	----------	----------

[1] Each patient is counted only once although he may have had a number of retests.
[2] This person, whose reaction changed from positive to negative, died 15 days after his change-over was observed.

Discussion

Depression of skin sensitivity has been reported on several occasions in patients critically ill with tuberculosis (*1*, *2*). Rich (*5*) considers this type of depression "specific" to tuberculosis. Declines of sensitivity reported with measles, other infections, cachetic states and pregnancy are considered by Rich to be "nonspecific."

The present study suggests that depression of skin sensitivity to both tuberculin and histoplasmin in critical illness is a function of critical illness itself—of whatever kind—and is not specific to a particular disease. A number of different diagnoses were represented among the 305 patients in this study, yet desensitization was general and the rate of reaction declined markedly as patients approached death.

One explanation which may be advanced for the low rate of skin sensitivity is that critical illness depresses the body's ability to react to any antigenic stimulus. Advancing age seems further to depress skin reactions, perhaps because decreased circulation weakens the skin's ability to react when the body is under critical attack. It is possible, on the other hand, that sensitivity tends to decline with age because of the debilitating effect of chronic diseases common among older people. The observation that the number of reactors declines markedly as a group of patients nears death suggests that the loss of skin sensitivity is part of the degeneration of all the physiological and immunological processes.

The decline of sensitivity is not specific to the disease from which a patient suffers or to the antigen used for testing. That the decline is nonspecific is supported by the observation of increased sensitivity among those who recovered from illness. Some 40 percent of these regained their ability to react to either antigen shortly after they began to improve. It seems probable, therefore, that returning health was the determining element in this conversion.

Conclusions

1. Critical illness exerts a depressing effect on skin sensitivity to tuberculin and to histoplasmin.

2. The depressing effect of critical illness on skin sensitivity becomes more marked with advancing age.

3. Patients with a fatal illness, particularly those who are within a few days of death, exhibit the lowest rate of skin sensivity.

4. Almost half (40 percent) of those insensitive when critically ill, reacted positively to skin tests again after they began to improve.

5. The evidence suggests that the depression is nonspecific with respect to the antigens used and to the cause of illness.

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6. These results call into question the value of any type of skin tests on persons critically ill from any cause.

ACKNOWLEDGMENT

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Variations in Histoplasmin Sensitivity in Certain Cities in Eastern Kansas [1]

By Ivan L. Bunnell, *Senior Assistant Surgeon*, and Michael L. Furcolow, *Surgeon*, *Public Health Service*

Previous studies have demonstrated the geographic distribution of histoplasmin sensitivity in the United States (*1*). In general, the distribution of histoplasmin reactors is concentrated in the central part of the country, with the western limits of the high prevalence area running through eastern Kansas (*2*). It is also known that the frequency of histoplasmin reactions decreases sharply at the periphery of the high prevalence area (*3*, *4*, *5*). It is the purpose of this paper to demonstrate that, as one moves westward of the high prevalence area in eastern Kansas, the frequency of these reactions continues to decrease progressively.

Materials and Methods

Surveys by means of skin tests have been made in Kansas City, Missouri, and its environs, and five cities in eastern Kansas: Lawrence, Topeka, Williamsburg, Ottawa, and Wichita during 1945, 1946, and 1947. Of the groups studied, Kansas City has had the most thorough coverage (*6*), therefore the histoplasmin sensitivity of representative age groups of its population is fairly well determined. In the other cities, smaller numbers of persons have been tested, but in each instance a fairly satisfactory estimate of the percentage of children positive to histoplasmin at different ages can be made. On the basis of these data it is possible to construct a sensitivity curve showing

[1] From the Office of Field Studies, Tuberculosis Control Division.

the percentage of positive reactors in each age group in each of the different cities.

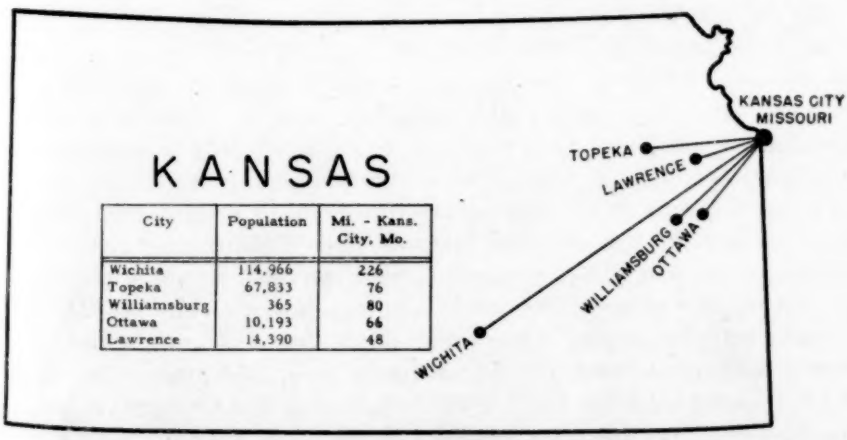
In Wichita, Topeka, and Lawrence the original plan was to test as many children as possible aged 6, 12, and 18 years. In practice, however, tests were performed not only on children of these ages but by school classes and consequently included children outside the originally selected categories. Moreover, in Williamsburg and Ottawa, all school children for whom consent could be obtained were tested.

The records of white children only are included in this report. All tests were performed by the intracutaneous Mantoux method, and all children were tested with both tuberculin and histoplasmin. Readings were made at 48 hours and the measurements of the areas of both erythema and induration were recorded in millimeters. All reactions in which induration measured 5 millimeters or more in diameter were considered positive.

Histoplasmin (H3 or H15) employed in these studies was furnished by Dr. Chester Emmons and Dr. Arden Howell of the Public Health Service. One-tenth cc. of a 1 to 1,000 dilution in buffer-saline was injected.

The present report does not include any consideration of the results of the tuberculin tests in cities involved in this study. Few positive reactors were found and the rates were comparable to those reported for Kansas City (*6*).

Since in earlier studies differences in sensitivity to histoplasmin were encountered (*6*) between "lifetime" residents of Kansas City and "nonlifetime" residents, only the records of "lifetime" residents of the respective cities are included in this analysis. For purposes



City	Population	Mi. - Kans. City, Mo.
Wichita	114,966	226
Topeka	67,833	76
Williamsburg	365	80
Ottawa	10,193	66
Lawrence	14,390	48

Figure 1

of this study a lifetime resident is one who has not lived away from the city of his birth more than 6 months at any one time.

One method of comparing the histoplasmin sensitivity of the various cities is by inspecting the slope of the curves which show sensitivity at selected ages (figure 2). A simpler method is to construct theoretical sensitivity curves based on various "annual conversion rates" which might be operating to give the observed percentages of positive reactors at each age. The "annual conversion rate," the yearly rate at which negative reactors change to positive reactors, for a particular city was determined by trial and error application of various rates until a rate was found which, when applied annually, resulted in a theoretical curve which approximated the actual observed curve for histoplasmin sensitivity for that city.

Results

The percentage of positive reactors by age in each of five cities in Kansas was used to construct a sensitivity curve for those cities. These sensitivity curves were compared with the curve for Kansas City, Missouri, a large metropolis on the western edge of the area of high histoplasmin sensitivity.

Table 1 and the chart show the sensitivity curves for Wichita, Topeka, Lawrence, Ottawa, Kansas City, and Williamsburg. It is apparent that only the curve for Williamsburg is higher than that for Kansas City. In descending order, the curves for the other cities are those for Ottawa, Lawrence, Topeka, and Wichita. It is also evident from the curves that histoplasmin sensitivity falls off rapidly to the west of Kansas City.

Theoretical annual conversion rates were calculated which approximated the observed age curves (table 2 and figure 2).

It can be seen from further study of the chart that it is not possible by the application of one annual conversion rate to duplicate the observed curves for all of the six cities studied. The curves for Wichita, Topeka, and Lawrence can each be roughly approximated by a single conversion rate, applied yearly (0.3, 1.8, and 3.2 percent per year respectively). The curves representing histoplasmin sensitivity by age for Kansas City, Ottawa, and Williamsburg cannot be duplicated by a single theoretical annual conversion rate applied for the entire 18 years. In order to approximate the observed histoplasmin rate by age in these cities it was necessary to apply two annual conversion rates of different magnitude, that among the older children being considerably higher than among the younger children. For Kansas City, the rates were 3.2 percent per year for the first 6 years and 7.5 percent per year thereafter. The Ottawa rate is quite similar, 3.2 percent per year for the first 7 years and 7 percent per year

Table 1. *Number and percent of positive reactors to histoplasmin in Kansas City, Mo., and five cities in eastern Kansas by age groups*

Age			1–4	5–6	7–8	9–10	11–12	13–14	15–16	17–18	Totals
Kansas City, Mo.	No. tested		289	1,201	1,157	1,137	1,114	1,384	1,462	288	8,033
	Histoplasmin positive	No.	23	180	295	434	506	762	886	200	3,286
		Percent	7.9	14.9	25.5	38.2	45.4	55.0	60.6	69.4	
Lawrence, Kans.	No. tested						22	87	62	14	185
	Histoplasmin positive	No.					6	34	26	6	72
		Percent					27.3	39.1	41.9	42.8	
Topeka, Kans.	No. tested			98	103	38	184	455	260	39	1,177
	Histoplasmin positive	No.		6	13	5	32	94	64	11	225
		Percent		6.1	12.6	13.2	17.4	20.7	24.6	28.2	
Wichita, Kans.	No. tested			149	142	43	132	29	306	158	959
	Histoplasmin positive	No.		2	2	3	5	2	15	7	36
		Percent		1.3	1.4	7.0	3.8	6.9	4.9	4.4	

Age			5–9	10–14	15–18	Totals
Ottawa, Kans.	No. tested		254	192	112	558
	Histoplasmin positive	No.	51	87	67	205
		Percent	20.7	45.3	59.8	
Williamsburg, Kans.	No. tested		27	38	25	90
	Histoplasmin positive	No.	10	26	21	57
		Percent	37.0	68.4	84.0	

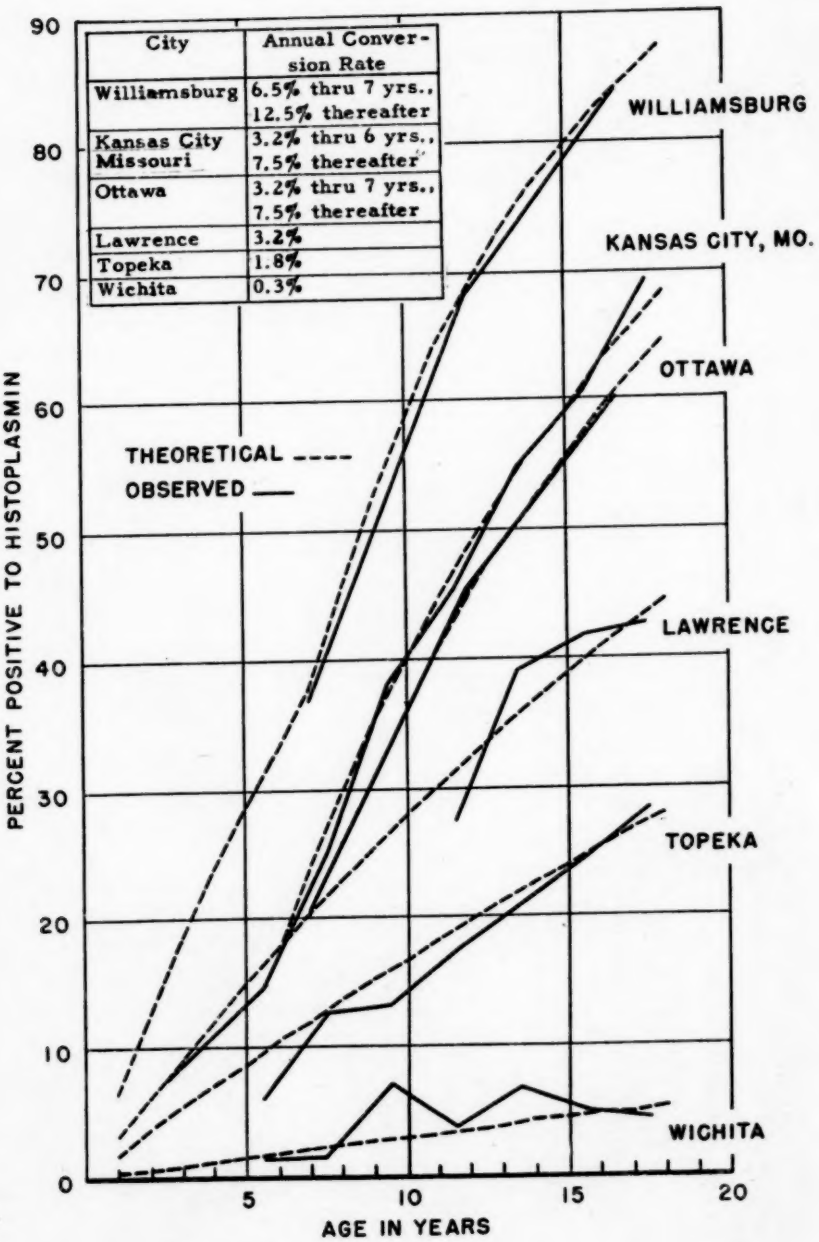

City
Annual Conversion Rate
Williamsburg
6.5% thru 7 yrs., 12.5% thereafter
Kansas City Missouri
3.2% thru 6 yrs., 7.5% thereafter
Ottawa
3.2% thru 7 yrs., 7.5% thereafter
Lawrence
3.2%
Topeka
1.8%
Wichita
0.3%
WILLIAMSBURG
KANSAS CITY, MO.
OTTAWA
LAWRENCE
TOPEKA
WICHITA
THEORETICAL
OBSERVED
PERCENT POSITIVE TO HISTOPLASMIN
AGE IN YEARS
0
10
20
30
40
50
60
70
80
90
5
10
15
20

Figure 2

Table 2. *Percent positive at various ages when different theoretical annual conversion rates are applied*

Year	ANNUAL CONVERSION RATES						
	0.3 percent	1.8 percent	3.2 percent	7.0 percent	7.5 percent	6.5 percent	12.5 percent
1	0.30	1.8	3.2	----------	----------	6.5	----------
2	0.6	3.6	6.5	----------	----------	12.6	----------
3	0.9	5.3	9.3	----------	----------	18.3	----------
4	1.2	7.0	12.2	----------	----------	23.6	----------
5	1.5	8.7	15.0	----------	----------	28.5	----------
6	1.8	10.3	17.7	→	17.7	33.2	----------
7	2.1	11.9	20.3	→ 20.3	23.9	37.5	→ 37.5
8	2.4	13.5	22.9	25.9	29.6	----------	45.3
9	2.7	15.1	25.4	31.1	34.9	----------	52.4
10	2.9	16.6	27.7	35.9	39.8	----------	58.6
11	3.2	18.1	30.1	40.4	44.3	----------	64.0
12	3.5	19.6	32.3	44.6	48.5	----------	68.8
13	3.8	21.0	34.5	48.5	52.3	----------	72.9
14	4.1	22.4	36.6	52.1	55.9	----------	76.6
15	4.4	23.8	38.6	55.4	59.2	----------	79.7
16	4.7	25.2	40.6	58.5	62.3	----------	82.5
17	4.9	26.5	42.5	61.4	65.1	----------	84.9
18	5.2	27.9	44.3	64.1	67.7	----------	87.1
19	5.5	29.2	46.1	66.6	70.1	----------	89.0
20	5.8	30.4	47.8	69.0	72.4	----------	90.7

thereafter. Williamsburg requires conversion rates of 6.5 percent per year for the first 7 years and 12.5 percent per year thereafter.

The Kansas City conversion rate is appreciably higher than the Lawrence rate although the cities are only 48 miles apart. The rate for Lawrence is in turn distinctly higher than that for Topeka, a city only 28 miles west. Wichita, 170 miles south of Topeka but only 90 miles west has a rate only one-sixth that of Topeka. A marked difference is also seen between Ottawa and Williamsburg which are only 14 miles apart.

Discussion

Data concerning the histoplasmin sensitivity for various cities are rendered more easily comparable by calculating the annual conversion rates which could be operating in each city. By this method interesting comparisons can be made between the cities in the eastern one-third of Kansas where studies were made. It is evident that there are marked differences in the rates of acquiring sensitivity within relatively small geographic areas. By and large, cities west of Kansas City, Missouri, have lower rates than Kansas City. In the case of Lawrence, Topeka, and Wichita—the farther west the city, the lower the rate. Ottawa, about as far west of Kansas City as Lawrence, but about 20 miles to the south, has a rate only slightly less than that of Kansas City. The reason for the difference between Ottawa's and Lawrence's rates is not apparent.

The rather marked differences between the rates for Ottawa and Williamsburg are based on a rather small number of observations in

Williamsburg. However, at each point, the differences are of the same degree. The differences may well be related to the fact that Ottawa is a small city of 10,193 population, whereas Williamsburg is a rural community. Williamsburg's higher rate is compatible with that of other rural communities which have somewhat higher histoplasmin rates than do urban areas (*3*, *4*).

It appears that a single yearly conversion rate serves to explain the observed curves in areas where the sensitivity is low, as in Wichita, Topeka, and Lawrence, whereas, in areas where the sensitivity is higher, two rates appear to be operating. For Kansas City, Ottawa, and Williamsburg, higher rates are needed to account for the percentage of positive reactors found in children over 6–7 years of age than in those under this age. In fact, the rate appears to be at least double after this age.

There are a number of possible explanations for this higher rate after the age of 6 or 7 years. Among these, two readily come to mind. The first is that the higher rate in older children may be due to different epidemic conditions prevailing, previous to the last 6 or 7 years or prior to 1939–40, with higher infection rates than have prevailed since these years. In other words, the infection must have been twice as prevalent in the years before 1939–40 as in the years since. The second possibility is that different rates are prevalent at different ages in the present population. This would imply some marked change in the exposure or environment of the child at about the age of 6 or 7. The most obvious change which occurs at this time is the child's entrance into school. This in turn suggests that person to person contact with other children at school may be a factor in transmission.

Summary

Studies of histoplasmin sensitivity in five cities in the eastern one-third of Kansas reveal that:

1. There is a rapid decrease in the frequency of positive reactors to the west of Kansas City, Missouri.

2. Calculations of the theoretical annual conversion rates or yearly rates of increase in new positive reactors facilitate comparison of histoplasmin sensitivity in these cities.

3. A single annual conversion rate appears to be acting at all ages through 18 in cities such as Wichita, Topeka, and probably Lawrence, where histoplasmin sensitivity is low. Where the rates are higher there appear to be two different rates operating, with the rates for children over 7 years of age being at least twice those for children under 7 years.

4. Further study is needed to determine more accurately the extent of the area of high histoplasmin sensitivity and to explain if possible the meaning of the sharp increase in reactor rates which occurs about the age of 7 years in areas of high sensitivity.

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Effect of Different Methods of Coagulation of Culture Media on Tubercle Bacilli Growth

By MARTIN M. CUMMINGS,[1] MARGARET C. DRUMMOND,[1] and GEORGE T. LEWIS [2]

Recent investigations have emphasized the importance of the inhibition of growth of the tubercle bacillus by traces of free fatty acid in the culture media. This suggested that the deleterious effect of overheating egg media was a possible explanation for the production of this inhibitory action. Dubos and Davis (*1*) called attention to the extreme sensitivity of tubercle bacilli to long-chain fatty acids in a medium (*2*) which contained Tween-80, a water-soluble ester of oleic acid. Davis and Dubos (*1*) showed that while the esterified fatty acid itself is nontoxic, and indeed serves as a nutrient, the commercial Tween-80 contains sufficient free fatty acid (*3*) to account for its toxicity.

The significance of free fatty acid in the medium was further emphasized by the following observations: (a) The function of albumin in permitting small inocula to grow in this medium depends upon its

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capacity to bind free fatty acids (*4*), the albumin thus acting as a protective rather than as a nutritive growth factor; (b) the deterioration of stored Tween-albumin medium is caused by hydrolysis of the ester by traces of lipase in the commercial albumin, a reaction which results in the liberation of toxic, free (unesterified) fatty acid (*3*); and (c) the slow deterioration of Tween-80 alone in aqueous solution is caused by its spontaneous hydrolysis, which is faster at higher temperatures (*5*).

Although these observations were restricted to Tween-albumin media, Corper (*6*) at the same time reported that the age of eggs used in the preparation of egg media affected the growth of tubercle bacilli, and ventured the suggestion that this was due to an increased fatty acid content of old eggs. He pointed out that there was a tendency toward the liberation from old eggs of fatty substances which would either coat the surface of the medium after sterilization, or would float on the water of condensation.

In view of these facts and the known high content in egg yolk of lipids containing esterified fatty acid, studies were instituted to determine the possible presence and relative concentration of free fatty acids or similar substances in lots of culture media prepared by inspissation and autoclaving.

Preparation of Media

The culture media employed throughout this study were the Lowenstein egg medium (*7*, *8*) (Jensen modification) and the Petragnani medium (*9*) (MacNabb modification). Both were prepared under aseptic conditions. Reagent grade chemicals, whole potato flour, fresh eggs (1–3 days old), and homogenized whole milk were employed in the preparation.

Coagulation of both media was accomplished by inspissating at 80°–85° C., and by autoclaving at a temperature of approximately 100° C., keeping all valves closed, except the steam inlet, thus retaining the original air content inside the autoclave. The time of coagulation was measured from the moment the desired temperature was reached and was varied within feasible limits, 90, and 40 minutes for inspissation, and 90, 40, 30, and 20 minutes for autoclaving. The 40-minute inspissation period is employed routinely by this laboratory for coagulation of egg media, whereas various other laboratories recommend 30 and 20 minutes for autoclaving. The 90-minute period was selected because it is the practice in some laboratories to sterilize for 30 minutes on three successive days. The bacteriological data are reported only for the media heated at 85° C. and 100° C. for 40 minutes.

The pH of Lowenstein-Jensen medium is neutral or faintly basic,

7.0–7.4, whereas that of Petragnani is approximately 6.8. Prior to coagulation the pH of each lot was determined by the use of a Beckman pH meter, but with a single exception, no attempt was made to alter the values obtained. In one set of experiments, the pH of the Lowenstein-Jensen medium was adjusted to 6.5, since, if oleic acid is a component of this ether-soluble acidic material, it is extractable only at a pH of 6.5 or less, but the variations in the results obtained fell within the range of experimental error, and no emphasis should be placed upon them.

Methods

Chemical—Davis (*10*), in 1947, described a method by which it is possible to estimate small amounts of free fatty acid in a liquid medium containing Tween-80. This procedure involved: (a) extracting the acidified material with ether; (b) testing for completeness of extraction by separately titrating an additional extraction at the end of a regular series and comparing it with the blank; (c) evaporating the ether by immersion in hot water; (d) dissolving the residue in 1.0 ml. of ethyl alcohol; and (e) titrating to an olive green end-point with N/50 aqueous NaOH, using 1 drop of 0.1 percent thymol blue as an indicator.

The necessity of modifying this procedure in applying it to solid egg media is obvious. For example, extraction by a piston-like motion of a long glass rod in an open test tube (*10*) would be ineffectual in the case of solid material. Therefore, the usual Soxhlet extraction apparatus for continuous liquid extraction from a solid was adopted instead. Also the use of thymol blue as an indicator was not desirable since its olive green end-point might be interfered with by the malachite green dye added to the culture medium as a contamination retardant. Phenolphthalein, an indicator active in the same pH range as thymol blue, was used, therefore, in order to avoid this color confusion. Parallel runs on media without malachite green, however, demonstrated that the dye has no effect upon such determinations, but to maintain comparable conditions, phenolphthalein was employed throughout the experiments.

For the purposes of these experiments, titrations were carried out, using 0.1 N and later 0.05 N NaOH, with a phenolphthalein as an indicator, the end-point being reached when the pink color persisted for 1 minute upon shaking. With the exception of the foregoing, only minor modifications were employed.

After preparation and coagulation by the various methods, the whole medium slant was removed from the test tube, placed into a tared Petri dish, and dried at 50° C. for approximately 24 hours in a hot-air oven. It was then finely pulverized in a mortar, and was again placed in the Petri dish in the oven for an additional period of

time. Since this time element seemed inconsequential, it was allowed to vary within the limits of several hours. The sample was left at least 12 hours in a desiccator, until it attained constant weight.

Aliquot samples of 500 mg. each were accurately weighed on an analytical balance, and extracted in a Soxhlet continuous extraction apparatus, using reagent grade ether. The extraction was continued for a minimum of 6 hours. To test for completeness of extraction, a separate ether supply was added, and the extraction repeated for 2 additional hours. Since the addititional extraction yielded an acid titer only as high as that of the alcohol blank, the extraction was deemed complete, and an approximately 7-hour extraction was adopted for all subsequent samples.

The solvent, containing all the ether extractable substances, was then quantitatively transferred to a small filter flask, and evaporated at room temperature, by means of a vacuum pump, until no odor of ether was detectable. At this point the residue was dissolved by the addition of 2.0 ml. of ethyl alcohol, and 2 drops of 1 percent phenolphthalein. It was then titrated with either 0.1 N or 0.05 N NaOH, until the pink color persisted for at least 1 minute after vigorous shaking. The shaking was accomplished manually at first, but later a stream of air, from which CO_2 had previously been removed by soda lime, was adopted to attain homogeneity. A blank was run routinely on 2.0 ml. of ethyl alcohol and this value subtracted from the sample titration value.

Ether extractions of the media prior to coagulation were also carried out, and these were accomplished by shaking 5.0 ml. of the liquid medium (without the addition of malachite green) with at least twice the volume of ether. The layers were allowed to separate, and the ether layer quantitatively transferred to a small flask. This was repeated a minimum of three times, the earliest samples being tested for completeness of extraction by determining the titer of a fourth extraction, and comparing it with the alcohol blank. The procedure for evaporation and titration, described above, was then followed as in the case of solid media.

Bacteriological—In order to test the growth promoting properties of the media used in this study, after sterilization by inspissation at 85° C. for 40 minutes and by autoclaving at 100° C. for 40 minutes, groups of 10 tubes of each medium prepared by these methods were inoculated with amounts of inoculum ranging from 10^{-5} mg./ml. to 10^{-7} mg./ml. The inoculum consisted of homogenous suspension of H37 Rv in physiological saline. Growth was studied by recording the rate of appearance and number of colonies which appeared.

In this series of tests, experiments with the Lowenstein-Jensen and Petragnani media, were made at different times, with different

batches of media and with lots of inocula prepared from different subcultures of the H37 Rv strain. While the individual results were not in exact agreement as to total colony counts, the trend in all was the same.

Results

Chemical—The results obtained, using the modified Davis extraction and titration method, on culture media before and after coagulation by both techniques for varying periods are given in tables 1, 2, 3. Table 1 shows that there is ether-extractable material present

Table 1. *Ether-extractable acid content of Lowenstein-Jensen medium prior to coagulation*

Sample No.	Mg. alkali required for neutralization of 5 ml. aliquots [1]
1	1. 13
2	1. 13
3	0. 93
4	1. 07
5	1. 13
6	1. 19
7	1. 13

[1] Air-dry weight 0.9 gm. average.

before heating. Table 2 points out the differences in the ether-extractable acid content of one lot of Lowenstein-Jensen and one lot of Petragnani egg media, the time of heating being varied between 20 and 90

Table 2. *Effect of different methods of coagulation on the ether-extractable acid content of Lowenstein-Jensen and Petragnani egg media*

Methods of coagulation	Time of coagulation	Mg. alkali required for neutralization of 1 gm. sample	
		Lowenstein-Jensen	Petragnani
Autoclaved	90	7. 7	9. 2
Autoclaved	90	7. 4	8. 3
Autoclaved	90	7. 2	----------
Inspissated	90	6. 8	6. 5
Inspissated	90	6. 1	7. 1
Inspissated	90	6. 5	6. 9
Autoclaved	40	7. 6	----------
Autoclaved	40	6. 9	----------
Autoclaved	40	7. 1	----------
Inspissated	40	3. 4	4. 1
Inspissated	40	3. 2	3. 7
Inspissated	40	3. 6	4. 4
Autoclaved	30	7. 3	6. 9
Autoclaved	30	6. 7	7. 2
Autoclaved	30	6. 4	7. 2
Autoclaved	20	----------	7. 1
Autoclaved	20	----------	6. 9

minutes. The results given in this table represent the limits of the range of variations in values obtained, each group of three figures containing the high, low, and a random middle value of as many as eight or nine determinations. The reproducibility of the method was thus proved, and the table shows the exact number of determinations performed. Table 3 compares the ether-extractable acid content of

Table 3. *Effect of different methods of coagulation on the ether-extractable acid content of Lowenstein-Jensen egg medium* [1]

Method of coagulation	Time of coagulation	Mg. alkali required for neutralization of 1 gm. sample	
		Without malachite green	Without malachite green and with pH adjusted
Autoclaved	40	6. 8	[2] 6. 9
Autoclaved	40	6. 6	[2] 6. 9
Inspissated	40	2. 6	2. 9
Inspissated	40	3. 0	3. 0
Inspissated	40	----------	[2] 3. 2
Inspissated	40	----------	[2] 3. 2
Autoclaved	20	6. 8	----------
Autoclaved	20	7. 2	----------

[1] This experiment represents 2 separate lots of culture media.
[2] The pH of these samples was adjusted to 6.5.

two different lots of Lowenstein-Jensen medium, each prepared without malachite green. The pH of half of one lot was adjusted to 6.5, to show the effect of an increased hydrogen-ion concentration.

It is obvious that the titration values, expressed as mg. of alkali required for neutralization of 1 gm. of dried sample, in the case of autoclaved media, are more than double those of inspissated material. In the case of the 90-minute inspissated media, however, the values were only slightly lower than the range of values obtained for autoclaved media.

Bacteriological—The growth obtained with the media studied as above noted is shown in table 4, which records typical data for different

Table 4. *Total colonies on 10 tubes of Lowenstein-Jensen culture medium inoculum 0.1 ml. of 10^{-4} and 10^{-5} mg./ml. H37 Rv*

Experiment	Inspissated 85° C. 40 min.		Autoclaved 100° C. 40 min.		pH
	10^{-4} mg./ml.	10^{-5} mg./ml.	10^{-4} mg./ml.	10^{-5} mg./ml.	
Exp. 1	850	590	495	345	7. 2
Exp. 2	105	14	86	10	7. 0
Exp. 3	370	225	190	69	6. 5

lots of Lowenstein-Jensen medium, and in a study (table 5) using Lowenstein-Jensen and Petragnani media inoculated from dilutions of the same homogenous suspension of H37 Rv. Growth was more abundant on the inspissated medium, and although not shown in the tables, growth was also more rapid.

Table 5. *Total colonies on 10 tubes of culture medium inoculum 0.1 ml. of 10^{-5} and 10^{-6} mg./ml. H37 Rv*

Medium	Inspissated 85° C. 40 min.		Autoclaved 100° C. 40 min.	
	10^{-5} mg./ml.	10^{-6} mg./ml.	10^{-5} mg./ml.	10^{-6} mg./ml.
Lowenstein-Jensen	53	9	22	0
Petragnani	28	7	7	0

Discussion

Examination of the tables will point to several interesting findings. Most significant is the fact that the ether-soluble acidic material in the medium is increased by heating. Time and temperature are both factors in this process because prolonged heating at 85° C. gives values approaching those obtained at 100° C. for shorter periods. On the other hand, variations in the time during which the medium is autoclaved, between 20 and 90 minutes, had no effect on the titration values.

Bacteriological growth experiments correlate very well with the chemical findings. The amount of growth obtained, as measured by the number of colonies, decreases as the amount of ether-soluble acidic material in the medium increases.

Summary and Conclusions

Experiments have been carried out which demonstrate:

1. Heating increases the amount of ether-soluble acid in the media described.

2. About twice as much of this ether-soluble acid is present after autoclaving at 100° C. as following inspissation at 85° C.

3. The growth of the H37 Rv strain of the tubercle bacillus is impaired as the content of the ether-soluble acidic material increases in the medium.

Variations in the sensitivity of certain complex organic media for the growth of tubercle bacilli may be due to differences in the procedures for the coagulation of such media. These coagulation procedures cause the liberation in the media of varying amounts of ether-soluble acidic material which appears to inhibit the growth of the tubercle bacilli.

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INCIDENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED SEPTEMBER 11, 1948

Summary

A net increase of 20 cases in the incidence of poliomyelitis brought the total for the current week to 1,527 cases, as compared with 906 for the 5-year (1943–47) median and 1,726 and 825, respectively, for the corresponding weeks of 1946 and 1947, the highest and lowest of the past 5 years. Of the 29 States and the District of Columbia reporting currently more than 10 cases, 19 States showed a combined increase of 208 cases (540 to 748), 10 reported a decline, 768 to 623, and 1 State, Pennsylvania, reported the same number (51) for each week. The 20 States reporting more than 13 cases (besides Pennsylvania) are as follows (last week's figures in parentheses): *Increases*—Ohio 79 (65), Michigan 57 (48), Wisconsin 48 (39), Minnesota 101 (90), Iowa 81 (53), Missouri 32 (12), Nebraska 56 (27), Kansas 31 (28), Virginia 46 (31), West Virginia 28 (12), Oklahoma 37 (14), Texas 57 (52), Washington 20 (9); *decreases*—New York 95 (101), New Jersey 50 (56), Indiana 33 (39), Illinois 71 (87), North Carolina 112 (138), South Carolina 20 (23), California 205 (264). Of 13,838 cases reported since March 20 (13,693 for the same period of 1946), 5,117 occurred in the Middle Atlantic and North Central areas (New York 660, Ohio 609, Illinois 509, Minnesota 550, Iowa 449), 3,235 in the South Atlantic (North Carolina 1,987), 2,372 in the South Central (Texas 1,344), and 2,495 in the Pacific area (California 2,314).

Only 6 cases of Rocky Mountain spotted fever were reported during the week (last week 27, 5-year median 18), in as many States—Kansas, Maryland, North Carolina, South Carolina, Tennessee, and Oklahoma. One case of smallpox was reported, in Oklahoma. Of 27 cases of infectious encephalitis reported in 13 States, 10 occurred in South Dakota, and 3 in North Dakota.

Deaths recorded during the week in 93 large cities in the United States totaled 7,842, as compared with 10,547 last week, 8,264 and 8,607, respectively, for the corresponding weeks of 1947 and 1946, and a 3-year (1945–47) median of 8,264. The total to date is 344,155, same period last year, 342,796. Infant deaths totaled 609, last week 736, 3-year median 690. The cumulative number is 24,775, as compared with 27,597 for the same period last year.

806362—48——3

Telegraphic case reports from State health officers for week ended September 11, 1948

[Leaders indicate that no cases were reported]

Division and State	Diphtheria	Encephalitis infectious	Influenza	Measles	Meningitis meningococcal	Pneumonia	Poliomyelitis	Rocky Mt. spotted fever	Scarlet fever	Smallpox	Tularemia	Typhoid and paratyphoid fever [d]	Whooping cough	Rabies in animals
NEW ENGLAND														
Maine	1			30		8	9		2			1	20	
New Hampshire							3						1	
Vermont				4			1						2	
Massachusetts	6	1		40		230	13		11				58	
Rhode Island				2		1	1		4					
Connecticut				13	1	28	7		4			1	2	
MIDDLE ATLANTIC														
New York	2	2	(b)	87	3	113	95		34			6	108	9
New Jersey	5		1	41	1	60	50		3				53	2
Pennsylvania	2	1	(b)	36	1		51		22			4	79	3
EAST NORTH CENTRAL														
Ohio	5		1	16	2	51	79		29			6	36	10
Indiana		1	11	2		7	33		16			2	14	7
Illinois	1	1		8	5	52	71		22			2	41	
Michigan	6			38	2	19	57		22			2	24	3
Wisconsin	2		1	73		2	48		7				63	
WEST NORTH CENTRAL														
Minnesota				1	1		101		7			2	6	
Iowa				2			81		5				8	
Missouri	4			2	4	8	32		11			2	5	
North Dakota		3		4			8		1				1	
South Dakota		10			1	3	10		2				1	
Nebraska		1		4			56		6				29	
Kansas	1	2	15	3		5	31	1	5				18	
SOUTH ATLANTIC														
Delaware							7							
Maryland	4			27		24	7	1	5			4	21	
District of Columbia				1		9	13		4				3	
Virginia	4		269	21	2	28	46		9		1	1	30	
West Virginia	3		3	6	1	5	28		11				7	
North Carolina	13			3			112	1	7			3	10	
South Carolina	19		162	15		55	20	1	3		1	4	46	
Georgia	9	1	20	1		5	12		7		2	7	5	5
Florida	9				1	5	9					1	2	1

EAST SOUTH CENTRAL														
Kentucky	3					24	12		12			6		19
Tennessee	8	1	8	4		30	13	1	11		2	6	18	
Alabama	15		12	5	1	17	13		5			2	5	4
Mississippi [a]	13	1	37	10	1	14	12		6				4	
WEST SOUTH CENTRAL														
Arkansas	3		44	2		11	7		9		1		22	1
Louisiana	3			2		24	8		2			5		
Oklahoma	1		27	7	2	12	37	1	4	1	1		6	4
Texas	16		301	146	2	55	57		16			8	91	24
MOUNTAIN														
Montana			1	2			7		1		2		3	
Idaho	3		9	2		3	2		[c] 3			2	1	
Wyoming			1	2		1	5		1				8	
Colorado	2		5	18		4	12					5	18	
New Mexico				1		4	3		1				3	
Arizona			14	3		11	9		1			1	1	1
Utah [a]	2			17		6	2				7		16	
Nevada														
PACIFIC														
Washington	1			17		7	20		12			4	10	
Oregon			4	32		10	12		1				9	
California	3	2	3	65	2	5	205		13			4	27	
Total	169	27	949	815	33	956	1,527	6	357	1	17	91	935	
Median 1943–47	239	21	654	543	73		906	18	795	2	14	166	2,137	
Year to date, 36 weeks	5,765	390	143,432	552,229	2,390		14,188	467	56,973	51	718	2,460	60,185	
Median 1943–47	8,010	446	193,473	540,027	6,402		7,047	407	100,121	279	629	3,296	91,006	
	(27th)		(30th)	(35th)	(37th)		(11th)		(32d)	(35th)		(11th)	(39th)	
Seasonal low week ends	July 10		July 31	Sept. 4	Sept. 18		Mar. 20		Aug. 14	Sept. 4		Mar. 20	Oct. 2	
Since seasonal low week	1,155		4,617	815	3,172		13,838		1,357	1		1,987	91,451	
Median 1943–47	1,746		3,276	543	8,854		6,650		2,746	2		2,672	113,053	

[a] Period ended earlier than Saturday.
[b] New York City and Philadelphia only, respectively.
[c] Including cases reported as streptococcal infections and septic sore throat.
[d] Including paratyphoid fever and salmonella infections; currently reported separately, as follows: Connecticut 1; New York (salmonella infection) 3; Maryland (salmonella infection) 1; South Carolina 1; Georgia 5; Kentucky 1; Louisiana 1; Texas 1; Colorado 1; Washington 4; California 4.

Alaska: Mumps 1; influenza 6; chickenpox 11; diphtheria 1; botulism 2.
Territory of Hawaii: Measles 3; whooping cough 12.

TERRITORIES AND POSSESSIONS

Puerto Rico

Notifiable diseases—5 weeks ended July 31, 1948.—During the 5 weeks ended July 31, 1948, cases of certain notifiable diseases were reported in Puerto Rico as follows:

Disease	Cases	Disease	Cases
Chickenpox	28	Syphilis	150
Diphtheria	28	Tetanus	7
Dysentery	3	Tetanus, infantile	1
Gonorrhea	265	Tuberculosis (all forms)	861
Influenza	585	Typhoid fever	8
Malaria	116	Typhus fever (murine)	1
Measles	194	Whooping cough	92
Poliomyelitis	2		

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended August 21, 1948.—During the week ended August 21, 1948, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		7		21	33	15	24	13	32	145
Diphtheria				7	3			1		11
Dysentery, bacillary				2						2
German measles				2	3		1	6	2	14
Influenza		31			4	1			1	37
Measles			2	88	53	11	16	21	24	215
Meningitis, meningococcus		1							1	2
Mumps		5		9	29	14	5	8	1	71
Poliomyelitis		1		1	5	16	8	17	5	53
Scarlet fever		4		11	12	4	1	2	4	38
Tuberculosis (all forms)		3	16	94	17	47	5		36	218
Typhoid and paratyphoid fever				14	1	1		2		18
Undulant fever				1					4	5
Venereal diseases:										
Gonorrhea		16	5	62	62	28	30	54	38	295
Syphilis		6	3	78	40	6		6	17	156
Other forms									1	1
Whooping cough		10		94	22	4	10	3		143

FINLAND

Notifiable diseases—June 1948.—During the month of June 1948, cases of certain notifiable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis	10	Paratyphoid fever	194
Diphtheria	174	Poliomyelitis	3
Dysentery	2	Scarlet fever	324
Gonorrhea	1,105	Syphilis	228
Malaria	25	Typhoid fever	21

JAPAN

Encephalitis, Japanese "B" (suspected).—During the week ended August 7, 1948, 340 cases of Japanese "B" encephalitis (suspected), with 47 deaths, were reported in Japan, of which 287 cases and 38 deaths were stated to have occurred in Tokyo. Through the month of June only 1 case had been reported this year. For the month of July, 20 cases were reported, 18 of which occurred during the week ended July 31.

Notifiable diseases—5 weeks ended July 31, 1948, and total reported for the year to date.—For the 5 weeks ended July 31, 1948, and for the year to date, certain notifiable diseases were reported in Japan as follows:

Disease	5 weeks ended July 31, 1948		Total reported for the year to date	
	Cases	Deaths	Cases	Deaths
Diphtheria	734	51	9,816	907
Dysentery, unspecified	3,859	998	6,423	1,564
Encephalitis, Japanese "B"	[1] 20	6	[1] 21	6
Gonorrhea	19,126	----	145,643	----
Influenza	115	----	2,375	----
Malaria	1,001	2	3,087	17
Measles	5,660	----	43,491	----
Meningitis, epidemic	138	36	1,321	328
Paratyphoid fever	459	14	1,642	70
Pneumonia	4,334	----	89,816	----
Scarlet fever	291	3	1,757	21
Smallpox	7	1	26	1
Syphilis	18,950	----	137,345	----
Tuberculosis	40,988	----	222,271	----
Typhoid fever	1,589	147	5,069	570
Typhus fever	23	2	451	33
Whooping cough	8,412	----	30,864	----

NOTE.—The above figures have been adjusted to include delayed and corrected reports.

[1] Suspected.

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-mentioned diseases, except yellow fever, during recent months. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday in each month.

Cholera

India—Bihar Province—Patna.—Information dated August 16, 1948, reports an outbreak of cholera in Patna, Bihar Province, India. Two hundred cases are stated to have been admitted to the hospital, and 50 deaths had been reported.

Plague

British East Africa—Kenya.—During the week ended August 14, 1948, 5 cases of plague were reported in Kenya, British East Africa. For the week ended August 21, 2 cases with 1 death were reported.

Portugal—Azores.—During the week ended July 24, 1948, plague was reported in the Azores as follows: One case at Feteiras de Ponta Delgada and 1 case at Rabo de Peixe, both localities about 14 kilometers from the port of Ponta Delgada.

Smallpox

Greece—Salonika.—During the period July 11-20, 1948, 3 cases of smallpox were reported in Salonika, Greece, and 1 case was reported during the period August 1–10.

Rhodesia (Northern).—For the week ended August 21, 1948, 105 cases of smallpox with 30 deaths were reported in Northern Rhodesia.

Venezuela.—For the week ended August 28, 1948, smallpox (alastrim) was reported in Venezuela as follows: In Santa Barbara, Barinas State, 21 cases; in Yaritagua, Yaracuy State, 29 cases.

Yellow Fever

Gold Coast—Accra.—The 2 fatal suspected cases of yellow fever reported in Accra on August 4 and August 13, respectively (Pub. Health Rep. Sept. 10, 1948, p. 1,213, and Sept. 24, 1,948, p. 1,282) have been confirmed.

DEATHS DURING WEEK ENDED SEPT. 4, 1948

[From the Weekly Mortality Index, issued by the National Office of Vital Statistics]

	Week ended Sept. 4, 1948	Corresponding week, 1947
Data for 93 large cities of the United States:		
Total deaths	10,547	7,629
Median for 3 prior years	7,914	
Total deaths, first 36 weeks of year	336,313	334,532
Deaths under 1 year of age	736	659
Median for 3 prior years	659	
Deaths under 1 year of age, first 36 weeks of year	24,166	26,861
Data from industrial insurance companies:		
Policies in force	70,923,141	67,183,347
Number of death claims	11,333	9,146
Death claims per 1,000 policies in force, annual rate	8.4	7.1
Death claims per 1,000 policies, first 36 weeks of year, annual rate	9.4	9.4

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